

We claim:

1. An isolated and purified polypeptide wherein the polypeptide (a) is a variant type 2 methionine aminopeptidase ("MetAP2"), (b) has dominant negative MetAP2 activity and (c) contains a translation domain.
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2. The isolated and purified polypeptide of claim 1 comprising a sequence which is at least 46% identical to SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:16, or a fragment thereof.
3. The isolated and purified polypeptide of claim 2 comprising SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:16, or a fragment thereof.
4. The isolated and purified polypeptide of claim 3 which consists essentially of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:16, or a fragment thereof.
5. The isolated and purified polypeptide of claim 4 which consists essentially of SEQ ID NO:12, wherein the histidine at position number 231 is replaced with an alanine.
6. An isolated and purified polynucleotide comprising a nucleotide sequence encoding the polypeptide of claim 1.
7. The isolated and purified polynucleotide of claim 6 wherein the isolated and purified polynucleotide encodes a peptide that comprises SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:16, or a fragment thereof.
8. The isolated and purified polynucleotide of claim 7 wherein the isolated and purified polynucleotide encodes a peptide that consists essentially of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 or SEQ ID NO:16, or a fragment thereof.
9. The isolated and purified polynucleotide of claim 8 wherein the isolated and purified polynucleotide comprises a sequence selected from the list consisting of SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:18.

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10. The isolated and purified polynucleotide of claim 9 wherein the purified polynucleotide comprises SEQ ID NO:9.

11. A vector containing an isolated and purified polynucleotide which encodes the polypeptide of claim 1.

12. The vector of claim 11 wherein the polypeptide is SEQ ID NO:6.

13. The vector of claim 12 wherein the polynucleotide consists of SEQ ID NO:9.

14. The vector of claim 13 wherein the polynucleotide is operably linked to a promoter which is selected from the list consisting of GAL1, CMV, GPD, an endothelial cell-specific promoter and an immune cell-specific promoter.

15. The vector of claim 14 wherein the vector is an adenovirus and the promoter is CMV.

16. A method of treating a cell comprising contacting the cell with a composition comprising an isolated and purified polypeptide, wherein the polypeptide is a variant MetAP2 that has dominant negative MetAP2 activity and contains a translation domain.

17. The method of claim 16 wherein the cell is in a subject.

18. The method of claim 17 wherein the subject suffers from a disease mediated by a fungal infection, cell proliferation, angiogenesis, decreased function of p53 or immune system activity.

19. The method of claim 18 wherein the subject is a human suffering from a disease mediated by angiogenesis.

20. A method of treating a cell comprising contacting the cell with a composition comprising an isolated and purified polynucleotide, wherein the polynucleotide encodes a variant MetAP2 that has dominant negative methionine MetAP2 activity and contains a translation domain.

22. The method of claim 21 wherein the cell is in a subject.

23. The method of claim 22 wherein the subject is a human patient suffering from a disease mediated by fungal infection, cell proliferation, angiogenesis, decreased function of p53 or immune system activity.

24. The method of claim 23 wherein the disease is a disease mediated by angiogenesis.

25. The method of claim 24 wherein the polynucleotide is part of an adenovirus vector and operably linked to a CMV promoter.

26. A method of identifying an agent that modulates the activity of MetAP2 comprising contacting a cell with the agent, wherein
(a) the cell contains a functional gene that encodes a MetAP2 and does not contain an operable naturally occurring chromosomal copy of a gene encoding a MetAP1, and
(b) the modulation activity of the agent is determined by measuring either the relative growth rate of the cell or the fluorescence emission of the cell.

27. The method of claim 26 wherein
(a) the cell is a yeast cell which comprises a gene encoding MetAP1 operably linked to a regulatable promoter, and
(b) the modulation activity of the agent is determined by comparing the growth rate of the yeast cell in the absence of MetAP1 expression to the growth rate of the yeast cell in the presence of MetAP1 expression.

28. The method of claim 26 wherein
(a) the cell is a mammalian cell which comprises a polynucleotide that further comprises a gene encoding a MetAP1 and a gene encoding a fluorescent protein, and
(b) the modulation activity of the agent is determined by measuring the fluorescence emission of the cell.

29. The method of claim 26 wherein the agent is a polynucleotide.

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30 A method of identifying effectors of MetAP2 activity comprising contacting a yeast cell with a polynucleotide and determining that the polynucleotide encodes an effector of MetAP2 activity, wherein

- 5 (a) the yeast cell comprises a functional gene that encodes a MetAP2 and a polynucleotide that encodes a dominant negative MetAP2,
- (b) the yeast cell does not contain an operable naturally occurring chromosomal copy of a gene encoding a MetAP1, and
- 10 (c) the determining step comprises comparing the growth rate of yeast cells that contains a polynucleotide that encodes an effector of MetAP2 activity with a yeast cell that does not contain a polynucleotide that encodes an effector of MetAP2 activity, wherein the growth rate of a yeast cell that contains a polynucleotide that encodes an effector of MetAP2 activity is greater than the growth rate of a yeast cell that does not contain a polynucleotide that encodes an effector of MetAP2 activity.

30 31 The method of claim 30 wherein the polynucleotide is a human polynucleotide.